10/560726 IAP9 Rec'd PCT/PTO 08 DEC 2005

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<120> Feedback-resistant mevalonate kinases

<130> Case 21788

<150> EP 03012294.9

<151> 2003-06-12

<160> 33

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<170> PatentIn version 3.2

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Gly Glu Gly Ile Arg Thr Thr Phe Ala Asn Leu Ser Gly Gly Ala Thr 50 55 60

Tyr Ser Leu Lys Leu Leu Ser Gly Phe Lys Ser Arg Leu Asp Arg Arg 65 70 75 80

Phe Glu Gln Phe Leu Asn Gly Asp Leu Lys Val His Lys Val Leu Thr 85 90 95

His Pro Asp Asp Leu Ala Val Tyr Ala Leu Ala Ser Leu Leu His Asp 100 105 110

Lys Pro Pro Gly Thr Ala Ala Met Pro Gly Ile Gly Ala Met His His 115 120 125

Leu Pro Arg Pro Gly Glu Leu Gly Ser Arg Thr Glu Leu Pro Ile Gly 130 135 140

Ala Gly Met Gly Ser Ser Ala Ala Ile Val Ala Ala Thr Thr Val Leu 145 150 155 160

Phe Glu Thr Leu Leu Asp Arg Pro Lys Thr Pro Glu Gln Arg Phe Asp Page 1 Arg Val Arg Phe Cys Glu Arg Leu Lys His Gly Lys Ala Gly Pro Ile 180 185 190

Asp Ala Ala Ser Val Val Arg Gly Gly Leu Val Arg Val Gly Gly Asn 195 200 205

Gly Pro Gly Ser Ile Ser Ser Phe Asp Leu Pro Glu Asp His Asp Leu 210 220

Val Ala Gly Arg Gly Trp Tyr Trp Val Leu His Gly Arg Pro Val Ser 230 235 240

Gly Thr Gly Glu Cys Val Ser Ala Val Ala Ala Ala His Gly Arg Asp 245 250 255

Ala Ala Leu Trp Asp Ala Phe Ala Val Cys Thr Arg Ala Leu Glu Ala 260 265 270

Ala Leu Leu Ser Gly Gly Ser Pro Asp Ala Ala Ile Thr Glu Asn Gln 275 280 285

Arg Leu Leu Glu Arg Ile Gly Val Val Pro Ala Ala Thr Gln Ala Leu 290 295 300

Val Ala Gln Ile Glu Glu Ala Gly Gly Ala Ala Lys Ile Cys Gly Ala 305 310 315 320

Gly Ser Val Arg Gly Asp His Gly Gly Ala Val Leu Val Arg Ile Asp 325 330 335

Asp Ala Gln Ala Met Ala Ser Val Met Ala Arg His Pro Asp Leu Asp 340 345 350

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Pro Arg Ala Gln Pro Leu Pro Gly Gln Gly 370

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<213> homo sapiens

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Phe Pro Glu Ile val Ala Pro Leu Leu Thr Ser Ile Asp Ala Ile Ser 265 Leu Glu Cys Glu Arg Val Leu Gly Glu Met Gly Glu Ala Pro Ala Pro 285

Glu Gln Tyr Leu Val Leu Glu Glu Leu Ile Asp Met Asn Gln His His 290 295 300

Leu Asn Ala Leu Gly Val Gly His Ala Ser Leu Asp Gln Leu Cys Gln 305 310 315 320

Val Thr Arg Ala Arg Gly Leu His Ser Lys Leu Thr Gly Ala Gly Gly 325 330 335

Gly Gly Cys Gly Ile Thr Leu Leu Lys Pro Gly Leu Glu Gln Pro Glu 340 345 350

Val Glu Ala Thr Lys Gln Ala Leu Thr Ser Cys Gly Phe Asp Cys Leu 355 360 365

Glu Thr Ser Ile Gly Ala Pro Gly Val Ser Ile His Ser Ala Thr Ser 370 375 380

Leu Asp Ser Arg Val Gln Gln Ala Leu Asp Gly Leu 385 390 395

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35 40 45

Val Ser Val Asn Leu Pro Asn Ile Gly Ile Lys Gln Val Trp Asp Val 50 60

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Glu Gln Tyr Leu Val Leu Glu Glu Leu Ile Asp Met Asn Gln His His 290 295 300

Leu Glu Cys Glu Arg Val Leu Gly Glu Met Val Ala Ala Pro Val Pro

Leu Asn Ala Leu Gly Val Gly His Asn Ser Leu Asp Gln Leu Cys Gln 305 320 310

Val Thr Ala Ala His Gly Leu His Ser Lys Leu Thr Gly Ala Gly Gly

Gly Gly Cys Gly Ile Thr Leu Leu Lys Pro Gly Leu Glu Gln Ala Thr 340 345 350

Val Glu Ala Ala Lys Gln Ala Leu Thr Ser Cys Gly Phe Asp Cys Trp 355 360 365

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<213> rat

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Val Ser Leu Asn Leu Pro Asn Val Gly Ile Lys Gln Val Trp Asp Val 50 60

Ala Thr Leu Gln Leu Leu Asp Thr Gly Phe Leu Glu Gln Gly Asp Val 65 70 75 80

Pro Ala Pro Thr Leu Glu Gln Leu Glu Lys Leu Lys Lys Val Ala Gly 85 90 95

Leu Pro Arg Asp Cys Val Gly Asn Glu Gly Leu Ser Leu Leu Ala Phe 100 105 110

Leu Tyr Leu Tyr Leu Ala Ile Cys Arg Lys Gln Arg Thr Leu Pro Ser 115 120 125

Leu Asp Ile Met Val Trp Ser Glu Leu Pro Pro Gly Ala Gly Leu Gly 130 140

Ser Ser Ala Ala Tyr Ser Val Cys Val Ala Ala Ala Leu Leu Thr Ala 145 150 150

Cys Glu Glu Val Thr Asn Pro Leu Lys Asp Arg Gly Ser Ile Gly Ser 165 170 175

Trp Pro Glu Glu Asp Leu Lys Ser Ile Asn Lys Trp Ala Tyr Glu Gly 180 185 190

Glu Arg Val Ile His Gly Asn Pro Ser Gly Val Asp Asn Ser Val Ser 195 200 205

Thr Trp Gly Gly Ala Leu Arg Tyr Gln Gln Gly Lys Met Ser Ser Leu 210 220

Lys Arg Leu Pro Ala Leu Gln Ile Leu Leu Thr Asn Thr Lys Val Pro 225 230 235 240

Arg Ser Thr Lys Ala Leu Val Ala Gly Val Arg Ser Arg Leu Ile Lys 245 250 255

Phe Pro Glu Ile Met Ala Pro Leu Leu Thr Ser Ile Asp Ala Ile Ser 260 265 270

Leu Glu Cys Glu Arg Val Leu Gly Glu Met Ala Ala Ala Pro Val Pro 275 280 285

Glu Gln Tyr Leu Val Leu Glu Glu Leu Met Asp Met Asn Gln His His 290 295 300

Leu Asn Ala Leu Gly Val Gly His Ala Ser Leu Asp Gln Leu Cys Gln 305 310 315 320

Val Thr Ala Ala His Gly Leu His Ser Lys Leu Thr Gly Ala Gly Gly 325 330 335

Gly Gly Cys Gly Ile Thr Leu Leu Lys Pro Gly Leu Glu Arg Ala Lys 340 345 350

Val Glu Ala Ala Lys Gln Ala Leu Thr Gly Cys Gly Phe Asp Cys Trp 355 360 365

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Asp Arg Leu Thr Leu Gln Leu Lys Asp Ile Ser Leu Glu Phe Ser Trp 50 60

Ser Leu Ala Arg Ile Lys Glu Ala Ile Pro Tyr Asp Ser Ser Thr Leu 70 75 80

Cys Arg Ser Thr Pro Ala Ser Cys Ser Glu Glu Thr Leu Lys Ser Ile 85 90 95

Ala Val Leu Val Glu Glu Gln Asn Leu Pro Lys Glu Lys Met Trp Leu 100 105 110

Ser Ser Gly Ile Ser Thr Phe Leu Trp Leu Tyr Thr Arg Ile Ile Gly 115 120 125

Phe Asn Pro Ala Thr Val Val Ile Asn Ser Glu Leu Pro Tyr Gly Ser 130 135 140

Gly Leu Gly Ser Ser Ala Ala Leu Cys Val Ala Leu Thr Ala Ala Leu 145 150 155 160

Leu Ala Ser Ser Ile Ser Glu Lys Thr Arg Gly Asn Gly Trp Ser Ser 165 170 175

Leu Asp Glu Thr Asn Leu Glu Leu Leu Asn Lys Trp Ala Phe Glu Gly 180 185 190

Glu Lys Ile Ile His Gly Lys Pro Ser Gly Ile Asp Asn Thr Val Ser 195 200 205

Ala Tyr Gly Asn Met Ile Lys Phe Cys Ser Gly Glu Ile Thr Arg Leu 210 220

Gln Ser Asn Met Pro Leu Arg Met Leu Ile Thr Asn Thr Arg Val Gly 235 240 Page 8

Arg Asn Thr Lys Ala Leu Val Ser Gly Val Ser Gln Arg Ala Val Arg 245 250 255

His Pro Asp Ala Met Lys Ser Val Phe Asn Ala Val Asp Ser Ile Ser 260 270

Lys Glu Leu Ala Ala Ile Ile Gln Ser Lys Asp Glu Thr Ser Val Thr 275 280 285

Glu Lys Glu Glu Arg Ile Lys Glu Leu Met Glu Met Asn Gln Gly Leu 290 295 300

Leu Leu Ser Met Gly Val Ser His Ser Ser Ile Glu Ala Val Ile Leu 305 310 320

Thr Thr Val Lys His Lys Leu Val Ser Lys Leu Thr Gly Ala Gly Gly 325 330 335

Gly Gly Cys Val Leu Thr Leu Leu Pro Thr Gly Thr Val Val Asp Lys 340 345 350

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Thr Ile Glu Leu Asp Phe Pro Asp Ile Ser Phe Asn His Lys Trp Ser 50 60

Ile Asn Asp Phe Asn Ala Ile Thr Glu Asp Gln Val Asn Ser Gln Lys
70 75 80
Page 9

Leu Ala Lys Ala Gln Gln Ala Thr Asp Gly Leu Ser Gln Glu Leu Val Ser Leu Leu Asp Pro Leu Leu Ala Gln Leu Ser Glu Ser Phe His Tyr His Ala Ala Phe Cys Phe Leu Tyr Met Phe Val Cys Leu Cys Pro His Ala Lys Asn Ile Lys Phe Ser Leu Lys Ser Thr Leu Pro Ile Gly Ala Gly Leu Gly Ser Ser Ala Ser Ile Ser Val Ser Leu Ala Leu Ala Met Ala Tyr Leu Gly Gly Leu Ile Gly Ser Asn Asp Leu Glu Lys Leu Ser Glu Asn Asp Lys His Ile Val Asn Gln Trp Ala Phe Ile Gly Glu Lys Cys Ile His Gly Thr Pro Ser Gly Ile Asp Asn Ala Val Ala Thr Tyr Gly Asn Ala Leu Leu Phe Glu Lys Asp Ser His Asn Gly Thr Ile Asn Thr Asn Asn Phe Lys Phe Leu Asp Asp Phe Pro Ala Ile Pro Met Ile Leu Thr Tyr Thr Arg Ile Pro Arg Ser Thr Lys Asp Leu Val Ala Arg Val Arg Val Leu Val Thr Glu Lys Phe Pro Glu Val Met Lys Pro Ile Leu Asp Ala Met Gly Glu Cys Ala Leu Gln Gly Leu Glu Ile Met Thr Lys Leu Ser Lys Cys Lys Gly Thr Asp Asp Glu Ala Val Glu Thr Asn Asn Glu Leu Tyr Glu Gln Leu Leu Glu Leu Ile Arg Ile Asn His Gly Leu Leu Val Ser Ile Gly Val Ser His Pro Gly Leu Glu Leu Ile Lys Page 10

Asn Leu Ser Asp Asp Leu Arg Ile Gly Ser Thr Lys Leu Thr Gly Ala 340 350

Gly Gly Gly Cys Ser Leu Thr Leu Leu Arg Arg Asp Ile Thr Gln 355 360

Glu Gln Ile Asp Ser Phe Lys Lys Leu Gln Asp Asp Phe Ser Tyr 370 375 380

Glu Thr Phe Glu Thr Asp Leu Gly Gly Thr Gly Cys Cys Leu Leu Ser 385 390 400

Ala Lys Asn Leu Asn Lys Asp Leu Lys Ile Lys Ser Leu Val Phe Gln 405 410 415

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Val Ile Val Met Ser Asp Ile Gly Thr Glu Arg Arg Trp Asn Leu Gln 50 55 60

Ser Leu Pro Trp Gln His Val Thr Val Glu Asn Val Gln His Pro Ala 65 70 75 80

Ser Ser Pro Asn Leu Asp Leu Leu Gln Gly Leu Gly Glu Leu Leu Lys 85 90 95

Asn Glu Glu Asn Gly Leu Ile His Ser Ala Met Leu Cys Thr Leu Tyr Page 11 Leu Phe Thr Ser Leu Ser Ser Pro Ser Gln Gly Cys Thr Leu Thr Ile 115 120 125

Ser Ser Gln Val Pro Leu Gly Ala Gly Leu Gly Ser Ser Ala Thr Ile 130 135 140

Ser Val Val Ala Thr Ser Leu Leu Leu Ala Phe Gly Asn Ile Glu 145 150 155 160

Pro Pro Ser Ser Asn Ser Leu Gln Asn Asn Lys Ala Leu Ala Leu Ile 165 170 175

Glu Ala Trp Ser Phe Leu Gly Glu Cys Cys Ile His Gly Thr Pro Ser 180 185 190

Gly Ile Asp Asn Ala Val Ala Thr Asn Gly Gly Leu Ile Ala Phe Arg 195 200 205

Lys Ala Thr Ala His Gln Ser Ala Met Lys Glu Phe Leu Lys Pro Lys 210 220

Asp Thr Leu Ser Val Met Ile Thr Asp Thr Lys Gln Pro Lys Ser Thr 225 230 235 240

Lys Lys Leu Val Gln Gly Val Phe Glu Leu Lys Glu Arg Leu Pro Thr 245 250 255

Val Ile Asp Ser Ile Ile Asp Ala Ile Asp Gly Ile Ser Lys Ser Ala 260 265 270

Val Leu Ala Leu Thr Ser Glu Ser Asp Lys Asn Ser Ser Ala Lys Lys 275 280 285

Leu Gly Glu Phe Ile Val Leu Asn Gln Lys Leu Leu Glu Cys Leu Gly 290 295 300

Val Ser His Tyr Ser Ile Asp Arg Val Leu Gln Ala Thr Lys Ser Ile 305 310 315 320

Gly Trp Thr Lys Leu Thr Gly Ala Gly Gly Gly Gly Cys Thr Ile Thr 325

Leu Leu Thr Pro Glu Cys Lys Glu Glu Glu Phe Lys Leu Cys Lys Glu 340 345 350

21788wo.ST25.txt Ser Leu Leu Ala His Lys Asn Ser Ile Tyr Asp Val Gln Leu Gly Gly 355 360 365

Pro Gly Val Ser Val Val Thr Asp Ser Asp Ser Phe Phe Pro Gln Tyr 370 380

Glu Ser Asp Phe Asp Phe Lys Lys Leu Asn Leu Leu Ser Lys Phe Asn 385 390 400

Lys Tyr Tyr Ile

<210> 8

<211> 335

<212> PRT

<213> Pyrococcus abyssi

<400> 8

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Asp Leu Arg Thr Tyr Val Arg Ala Glu Phe Asn Asp Ser Gly Asn Ile 35 40 45

Lys Ile Glu Ala His Asp Ile Lys Thr Pro Gly Leu Ile Val Ser Phe 50 60

Ser Glu Asp Lys Ile Tyr Phe Glu Thr Asp Tyr Gly Lys Ala Ala Glu 65 70 75 80

Val Leu Ser Tyr Val Arg His Ala Ile Glu Leu Val Leu Glu Glu Ala 85 90 95

Asp Lys Arg Thr Gly Val Ser Val Ser Ile Thr Ser Gln Ile Pro Val
100 105 110

Gly Ala Gly Leu Gly Ser Ser Ala Ala Val Ala Val Ala Thr Ile Gly 115 120 125

Ala Val Ser Lys Leu Leu Asp Leu Glu Leu Ser Lys Glu Glu Ile Ala 130 135 140

Lys Met Gly His Lys Val Glu Leu Leu Val Gln Gly Ala Ser Ser Gly 145 150 155 160

21788wo.ST25.txt Ile Asp Pro Thr Val Ser Ala Ile Gly Gly Phe Leu Tyr Tyr Lys Gln 165 Gly Glu Phe Glu His Leu Pro Phe Val Glu Leu Pro Ile Val Val Gly Tyr Thr Gly Ser Ser Gly Ser Thr Lys Glu Leu Val Ala Met Val Arg 200 205 Arg Arg Tyr Glu Glu Met Pro Glu Leu Ile Glu Pro Ile Leu Glu Ser 210 Met Gly Lys Leu Val Asp Lys Ala Lys Glu Val Ile Ile Ser Lys Leu 225 240 Asp Glu Glu Lys Phe Leu Lys Leu Gly Glu Leu Met Asn Ile Asn 245 250 255 His Gly Leu Leu Asp Ala Leu Gly Val Ser Thr Lys Lys Leu Ser Glu 260 Leu Val Tyr Ala Ala Arg Thr Ala Gly Ala Ile Gly Ala Lys Leu Thr Gly Ala Gly Gly Gly Cys Met Tyr Ala Leu Ala Pro Gly Lys Gln 290 300 Arg Glu Val Ala Thr Ala Ile Lys Ile Ala Gly Gly Thr Pro Met Ile 305 310 315 320 310 Thr Arg Ile Ser Lys Glu Gly Leu Arg Ile Glu Glu Val Arg Glu <210> <211> 335 <212> PRT <213> Pyrococcus horikoshii <400> 9 Met Val Lys Tyr Val Leu Ala Ser Ala Pro Ala Lys Val Ile Leu Phe

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Glu Leu Arg Thr Tyr Val Arg Ala Gln Phe Asn Asp Ser Gly Asn Ile

Page 14

21788wo.ST25.txt Lys Ile Glu Ala His Asp Ile Lys Thr Pro Gly Leu Ile Val Ser Phe Ser Glu Asp Lys Ile Tyr Phe Glu Thr Asp Tyr Gly Lys Ala Ala Glu Val Leu Ser Tyr Val Arg Tyr Ala Ile Glu Leu Ala Leu Glu Glu Ser 90 Asp Lys Arg Val Gly Ile Asp Val Ser Ile Thr Ser Gln Ile Pro Val 100 Gly Ala Gly Leu Gly Ser Ser Ala Ala Val Ala Val Ala Thr Ile Gly Ala Val Ser Arg Leu Leu Gly Leu Glu Leu Ser Lys Glu Glu Ile Ala 130 140 Lys Leu Gly His Lys Val Glu Leu Leu Val Gln Gly Ala Ser Ser Gly 145 160 150 Ile Asp Pro Thr Val Ser Ala Val Gly Gly Phe Leu Tyr Tyr Lys Gln 165 Gly Lys Phe Glu Pro Leu Pro Phe Met Glu Leu Pro Ile Val Val Gly 180 185 190 Tyr Thr Gly Ser Thr Gly Ser Thr Lys Glu Leu Val Ala Met Val Arg 200 205 Lys Arg Tyr Glu Glu Met Pro Glu Leu Val Glu Pro Ile Leu Glu Ala 220 215 Met Gly Lys Leu Val Asp Lys Ala Lys Glu Ile Ile Leu Ser Lys Leu **225** -230 240 Asp Glu Glu Lys Leu Thr Lys Leu Gly Glu Leu Met Asn Ile Asn His Gly Leu Leu Asp Ala Leu Gly Val Ser Thr Lys Lys Leu Gly Glu 265 260 Leu Val Tyr Ala Ala Arg Thr Ala Gly Ala Ile Gly Ala Lys Leu Thr

Gly Ala Gly Gly Gly Cys Met Tyr Ala Leu Ala Pro Gly Arg Gln

290

Arg Glu Val Ala Thr Ala Ile Lys Ile Ala Gly Gly Ile Pro Met Ile 305 310 315 320

Thr Arg Val Ser Arg Glu Gly Leu Arg Ile Glu Glu Val Ser Arg 325 330 335

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<211> 334

<212> PRT

<213> Pyrococcus furiosus

<400> 10

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His Ser Val Val Tyr Gly Lys Pro Ala Ile Ala Ala Ile Asp Leu 20 25 30

Arg Thr Phe Val Glu Ala Glu Leu Ile Arg Glu Lys Lys Ile Arg Ile 35 40 45

Glu Ala His Asp Ile Lys Val Pro Gly Leu Thr Val Ser Phe Ser Glu
50 55 60

Asn Glu Ile Tyr Phe Glu Thr Asp Tyr Gly Lys Ala Ala Glu Val Leu 70 75 80

Ser Tyr Val Arg Glu Ala Ile Asn Leu Val Leu Glu Glu Ala Asp Lys 85 90 95

Lys Asn Val Gly Ile Lys Val Ser Ile Thr Ser Gln Ile Pro Val Gly 100 105 110

Ala Gly Leu Gly Ser Ser Ala Ala Val Ala Val Ala Thr Ile Gly Ala 115 120 125

Val Ser Lys Leu Leu Gly Leu Glu Leu Ser Lys Glu Glu Ile Ala Lys 130 135 140

Met Gly His Lys Thr Glu Leu Leu Val Gln Gly Ala Ser Ser Gly Ile 145 150 155 160

Asp Pro Thr Val Ser Ala Ile Gly Gly Phe Ile Phe Tyr Glu Lys Gly 165 170 175

Lys Phe Glu His Leu Pro Phe Met Glu Leu Pro Ile Val Val Gly Tyr 180 185 190

Thr Gly Ser Ser Gly Pro Thr Lys Glu Leu Val Ala Met Val Arg Lys 195 200 205

Arg Tyr Glu Glu Met Pro Glu Leu Ile Val Pro Ile Leu Glu Ala Met 210 220

Gly Lys Val Val Glu Lys Ala Lys Asp Val Ile Leu Ser Asn Val Asp 235 240

Lys Glu Glu Lys Phe Glu Arg Leu Gly Val Leu Met Asn Ile Asn His 245 250 255

Gly Leu Leu Asp Ala Leu Gly Val Ser Thr Lys Lys Leu Ser Glu Leu 260 265 270

Val Tyr Ala Ala Arg Val Ala Gly Ala Leu Gly Ala Lys Ile Thr Gly 275 280 285

Ala Gly Gly Gly Cys Met Tyr Ala Leu Ala Pro Asn Lys Gln Arg 290 295 300

Glu Val Ala Thr Ala Ile Arg Ile Ala Gly Gly Thr Pro Met Ile Thr 305 310 315 320

Glu Ile Ser Arg Glu Gly Leu Lys Ile Glu Glu Val Ile Lys 325

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His Ala Val Val Tyr Ser Lys Pro Ala Ile Ala Ala Ile Asp Arg 20 25 30

Arg Val Thr Val Thr Val Ser Glu Ser Ser Ser Thr His Val Thr Ile 35 40 45

Pro Ser Leu Gly Ile Arg His Ser Ser Glu Arg Pro Ser Gly Gly Ile 50 60

Leu Asp Tyr Ile Gly Arg Cys Leu Glu Leu Tyr His Asp Ala Ser Pro 75 80

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His Gly Arg Asp His Gly Pro Gly Glu Thr Ala Ala Arg Ala His Arg 115 120 125

Val Glu Val Asp Val Gln Gly Ala Ala Ser Pro Leu Asp Thr Ala Ile 130 135 140

Ser Thr Tyr Gly Gly Leu Val Tyr Leu Asp Ser Gln Arg Arg Val Arg 145 150 155 160

Gln Phe Glu Ala Asp Leu Gly Asp Leu Val Ile Ala His Leu Asp Tyr 165 170 175

Ser Gly Glu Thr Ala Arg Met Val Ala Gly Val Ala Glu Arg Phe Arg 180 185 190

Arg Phe Pro Asp Ile Met Gly Arg Ile Met Asp Thr Val Glu Ser Ile 195 200 205

Thr Asn Thr Ala Tyr Arg Glu Leu Leu Arg Asn Asn Thr Glu Pro Leu 210 215 220

Gly Glu Leu Met Asn Leu Asn Gln Gly Leu Leu Asp Ser Met Gly Val 235 230 240

Ser Thr Arg Glu Leu Ser Met Met Val Tyr Glu Ala Arg Asn Ala Gly 245 250 255

Ala Ala Gly Ser Lys Ile Thr Gly Ala Gly Gly Gly Gly Ser Ile Ile 260 265 270

Ala His Cys Pro Gly Cys Val Asp Asp Val Val Thr Ala Leu Asn Arg 275 280 285

Asn Trp Lys Ala Met Arg Ala Glu Phe Ser Val Lys Gly Leu Ile 290 295 300

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<211> 284

<212> PRT

<213> Archaeoglobus fulgidus

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Page 19

Cys Ile Phe Gly Leu Phe Lys Gly Glu Lys Pro Lys Gly Ser Phe Ile 260 270

Val Glu Pro Glu Lys Glu Gly Val Arg Ile Glu Glu 275 280

<210> 13

<211> 312

<212> PRT

<213> Methanococcus jannaschii

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Val Val Tyr Gly Tyr Arg Ala Ile Ser Met Ala Ile Asp Leu Thr Ser 20 25 30

Thr Ile Glu Ile Lys Glu Thr Gln Glu Asp Glu Ile Ile Leu Asn Leu 35 40 45

Asn Asp Leu Asn Lys Ser Leu Gly Leu Asn Leu Asn Glu Ile Lys Asn 50 60

Ile Asn Pro Asn Asn Phe Gly Asp Phe Lys Tyr Cys Leu Cys Ala Ile65707580

Lys Asn Thr Leu Asp Tyr Leu Asn Ile Glu Pro Lys Thr Gly Phe Lys 90 95

Ile Asn Ile Ser Ser Lys Ile Pro Ile Ser Cys Gly Leu Gly Ser Ser 100 105 110

Ala Ser Ile Thr Ile Gly Thr Ile Lys Ala Val Ser Gly Phe Tyr Asn 115 120 125

Lys Glu Leu Lys Asp Asp Glu Ile Ala Lys Leu Gly Tyr Met Val Glu 130 135 140

Lys Glu Ile Gln Gly Lys Ala Ser Ile Thr Asp Thr Ser Thr Ile Thr 145 150 155 160

Tyr Lys Gly Ile Leu Glu Ile Lys Asn Asn Lys Phe Arg Lys Ile Lys 165 170 175

Gly Glu Phe Glu Glu Phe Leu Lys Asn Cys Lys Phe Leu Ile Val Tyr 180 185 190 Page 20

Ala Glu Lys Arg Lys Lys Thr Ala Glu Leu Val Asn Glu Val Ala 195 200 205

Lys Ile Glu Asn Lys Asp Glu Ile Phe Lys Glu Ile Asp Lys Val Ile 210 215 220

Asp Glu Ala Leu Lys Ile Lys Asn Lys Glu Asp Phe Gly Lys Leu Met 225 230 235 240

Thr Lys Asn His Glu Leu Leu Lys Lys Leu Asn Ile Ser Thr Pro Lys 245 250 255

Leu Asp Arg Ile Val Asp Ile Gly Asn Arg Phe Gly Phe Gly Ala Lys 260 265 270

Leu Thr Gly Ala Gly Gly Gly Cys Val Ile Ile Leu Val Asn Glu 275 280 285

Glu Lys Glu Leu Leu Lys Glu Leu Asn Lys Glu Asp Val Arg 290 295 300

Ile Phe Asn Cys Arg Met Met Asn 305

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<211> 324

<212> PRT

<213> Aeropyrum pernix

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Gly Glu His Phe Val Val Arg Gly Ser Leu Ala Ile Val Ala Ala Ile 20 25 30

Gly Arg Arg Leu Arg Val Thr Val Arg Ser Gly Gly Lys Gly Ile Val 35 40 45

Leu Glu Ser Ser Met Leu Gly Arg His Ser Ala Pro Leu Pro Gly Gln
50 55 60

Gly Ala Ala Lys Val Ser Pro Val Leu Glu Pro Tyr Ile Ala Val 65 70 75 80

Leu Arg Ser Leu Ala Ala Arg Gly Tyr Ser Val Val Pro His Thr Ile 85 90 95 Page 21

Leu Val Glu Ser Gly Ile Pro Pro Arg Ala Gly Leu Gly Ser Ser Ala 100 105 110

Ala Ser Met Val Ala Tyr Ala Leu Ser Tyr Ser Ala Met His Gly Asp 115 120 125

Pro Leu Ser Ala Glu Asp Leu Tyr Ser Val Ala Met Glu Gly Glu Lys 130 135 140

Ile Ala His Gly Lys Pro Ser Gly Val Asp Val Thr Ile Ala Val Arg 145 150 155 160

Gly Gly Val Leu Ala Tyr Arg Arg Gly Glu Asn Pro Val Asp Ile Arg 165 170 175

Pro Gly Leu Thr Gly Val Thr Leu Leu Val Ala Asp Thr Gly Val Glu 180 185 190

Arg Arg Thr Arg Asp Val Val Glu His Val Leu Ser Ile Ala Asp Ala 195 200 205

Leu Gly Glu Ala Ser Thr Tyr Ile Tyr Arg Ala Ala Asp Leu Ile Ala 210 220

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